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# Total Urinary Isothiocyanates, Glutathione S-Transferase M1 Genotypes, and Lung Cancer Risk: A Preliminary Nested Case-Control Study in Taiwan

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**Background:** This study was conducted as a preliminary examination of the relationship between urinary ITC levels and lung cancer risk, and the effect of polymorphisms in the *GSTM1* gene on this ITC-associated risk. **Methods:** A nested case-control study using a urinary biomarker of total dietary intake of ITCs was performed. Thirty histologically confirmed lung cancer cases, ascertained by computerized linkage of data with information from the National Cancer Registry, were randomly selected from lung cancer cases in a 7-township cancer-screening cohort in Taiwan. Two cancer-free controls were matched to each case by age (±2 years), sex, residence, and date of collection of biologic specimens (±3 months). Total urinary ITC was measured by high-performance liquid chromatography, and homozygous deletion of the *GSTM1* gene was determined by PCR. **Results:** The percentage of individuals with undetectable ITC in the urine was 20% for cases and 11.7% for controls. Individuals with detectable ITC had a 50% decreased lung cancer risk (adjusted OR=0.5, 95% CI=0.2-1.7). Furthermore, the decreased risk associated with detectable urinary ITC was restricted to individuals with a *GSTM1*-null genotype. **Conclusions:** ITCs appear to be associated with a non-statistically significant reduced lung cancer risk in this Chinese population in Taiwan. The GST metabolic genotype modified the protective effect of ITCs on lung cancer risk. Further studies are needed to confirm the findings from this exploratory study.

Key words: glutathione S-transferase M1, isothiocyanates, lung cancer, nested case-control study

## INTRODUCTION

Numerous epidemiological studies indicate that consumption of large quantities of vegetables and fruit, particularly cruciferous vegetables (e.g., broccoli, cabbage, and brussels sprouts), is associated with a reduced incidence of cancer, notably cancer of the lung and colorectum[1,2]. Recently, there has been considerable interest in the cancer-protective effects of cruciferous vegetables. These vegetables contain a variety of biologically active constituents, many of which are postulated to play a part in cancer protection[3]. Among these, the isothiocyanates (ITCs) are efficacious chemopreventive agents for tumorigenesis induced by a variety of carcinogens at a number of organ sites[4]. In particular, experimental studies in animals have demonstrated the efficacy of ITCs in inhibiting lung carcinogenesis by known carcinogens[5,6]. Indeed, epidemiological evidence for the relationship between cruciferous vegetables and lung cancer is compelling[3,7]. One proposed mechanism for the chemopreventive effects of ITCs is through the down-regulation of cytochrome P-450 biotransformation enzyme levels and direct inhibition of their catalytic activities, together with induction of phase II enzymes that detoxify electrophilic metabolites from the phase I enzymatic activity[6].

Human glutathione S-transferases (GSTs) are phase II enzymes that play a critical role in the detoxification of many reactive electrophilic compounds by conjugation with glutathione (GSH). Thus, deficiency in GST isoenzyme activity may predispose an individual to the effects of electrophilic carcinogens. To date the human cytosolic GST superfamily contains at least 16 genes subdivided

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